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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/447,681	11/23/1999	JACK A. ROTH	INRP.003--2/	4103

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EXAMINER	
CROUCH, DEBORAH	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 06/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/447,681	ROTH, JACK A.	
	Examiner	Art Unit	
	Deborah Crouch, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *67 and 86-89* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *67 and 86-89* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 November 1999* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicant's arguments filed February 12, 2004 have been fully considered but are not persuasive. The amendment has been entered. Claims 67 and 86-89 are pending.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 67 and 86 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 22 and 37 of copending Application No. 08/626,678. Although the conflicting claims are not identical, they are not patentably distinct from each other because present claims 67 and 86 are obvious variations.

The present claims are to pharmaceutical compositions comprising adenoviral vectors comprising a wild-type p53 gene operably linked to a promoter (claim 86) and where the promoter is a CMV (claim 67). Claims 22 and 37 of '678 are drawn to recombinant adenovirus, which carries an adenovirus vector construct comprising an expression region encoding p53 under the control a CMV IE promoter and an adenovirus vector construct comprising an expression region encoding p53 under the control a CMV IE promoter. The pharmaceutical composition of present claims 67 and 86 contains the same recombinant adenovirus as claim 22 of '678, and the same p53 expression region and promoter as in claim 37 of '678. The CMV promoter of present claims 67 and 86 encompasses the CMV IE

promoter of claims 22 and 37 of '678. Further, the specification of '678 defines the claimed recombinant adenovirus and adenovirus construct as pharmaceutical compositions. Thus at the time of the instant invention, it would have been obvious to the ordinary artisan to make the claimed adenovirus vectors of present claims 67 and 86 given claims 22 and 37 of '678.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 67 and 86 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 5, 8-10, 12 and 15-18 of U.S. Patent No. 6,410,010 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because present claims 67 and 86 are obvious variations.

The present claims are to pharmaceutical compositions comprising adenoviral vectors comprising a wild-type p53 gene operably linked to a promoter (claim 86) and where the promoter is a CMV (claim 67). Claims 1-3, 5, 8-10 and 15-18 of '010 are drawn to recombinant adenovirus which carries an adenovirus vector construct comprising an expression region encoding p53 under the control a CMV IE promoter. The pharmaceutical composition of present claims 67 and 86 contains the same recombinant adenovirus as claims 1-3, 5, 8-10 and 15-18 of '010. The CMV promoter of present claims 67 and 86 encompasses the CMV IE promoter of claims 1-3, 5, 8-10 and 15-18 of '010. The limitations to expression levels in claims 1-3, 5, 8-10 and 15-18 of '010 are inherent properties of the virus and thus the adenovirus vectors of present claims 67 and 86 would also posses these properties. Thus at the time of the instant invention, it would have been obvious to the ordinary artisan to make the claimed adenovirus vectors of present claims 67 and 86 given claims 1-3, 5, 8-10 and 15-18 of '010.

Claims 86-89 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 12 of U.S. Patent No. 6,410,010 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because present claims 86-89 are obvious variations.

The present claim is to pharmaceutical compositions comprising adenoviral vectors comprising a wild-type p53 gene operably linked to a promoter (claim 86) and where the promoter is a β-actin, SV40 or RSV (claims 87-89). Claim 12 of '010 is drawn to recombinant adenovirus, which carries an adenovirus vector construct comprising an expression region encoding p53 under the control a promoter. The pharmaceutical composition of present claims 86-89 contains the same recombinant adenovirus as encompassed in claim 12 of '010. The specification of '010 defines promoter as including the β-actin, SV40 and RSV promoters. The limitation to expression levels in claim 12 of '010 is an inherent property of the virus and thus the adenovirus vectors of present claims 86-89 would also posses these properties. Thus at the time of the instant invention, it would have been obvious to the ordinary artisan to make the claimed adenovirus vectors of present claims 86-89 given claim 12 of '010.

Claims 67 and 86 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 7 and 12 of U.S. Patent No. 6,511,847 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because present claims 67 and 86 are obvious variations..

The present claims are to pharmaceutical compositions comprising adenoviral vectors comprising a wild-type p53 gene operably linked to a promoter (claim 86) and where the promoter is a CMV (claim 67). Claims 1, 7 and 12 of '847 are drawn to an adenovirus expression vector comprising an adenovirus expression vector comprising an ITR and a p53 gene under the control of a CMV promoter. The pharmaceutical composition of present

claims 67 and 86 contains the same adenovirus expression vector as claims 1, 7 and 12 of '847. An ITR is an inherent component of the adenovirus genome and would be present in the adenovirus vector in present claims 67 and 86 unless specifically deleted, which the claims does not so delete. Thus at the time of the instant invention, it would have been obvious to the ordinary artisan to make the claimed adenovirus vectors of present claims 67 and 86 given claims 1, 7 and 12 of '847.

Claims 67 and 86 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 7 and 12 of U.S. Patent No. 6,511,847 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because present claims 67 and 86 are obvious variations..

The present claims are to pharmaceutical compositions comprising adenoviral vectors comprising a wild-type p53 gene operably linked to a promoter (claim 86) and where the promoter is a CMV (claim 67). Claims 1, 7 and 12 of '847 are drawn to an adenovirus expression vector comprising an adenovirus expression vector comprising an ITR and a p53 gene under the control of a CMV promoter. The pharmaceutical composition of present claims 67 and 86 contains the same adenovirus expression vector as claims 1, 7 and 12 of '847. An ITR is an inherent component of the adenovirus genome and would be present in the adenovirus vector in present claims 67 and 86 unless specifically deleted, which the claims does not so delete. Thus at the time of the instant invention, it would have been obvious to the ordinary artisan to make the claimed adenovirus vectors of present claims 67 and 86 given claims 1, 7 and 12 of '847.

Claims 67 and 86 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 64 and 78 of U.S. Patent No. 6,740,320 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because present claims 67 and 86 are obvious variations.

The present claims are to pharmaceutical compositions comprising adenoviral vectors comprising a wild-type p53 gene operably linked to a promoter (claim 86) and where the promoter is a CMV (claim 67). Claims 64 and 78 of '320 are drawn to a pharmaceutical composition comprising a recombinant adenovirus containing an adenovirus vector construct comprising an expression region encoding p53 under the control a CMV promoter and a pharmaceutically acceptable carrier, expedient or diluent. The pharmaceutical composition of present claims 67 and 86 contains the same recombinant adenovirus as claims 64 and 78 of '320. Pharmaceutically acceptable carriers were known in the art at the time of filing and it would be obvious use them in the production of present claims 67 and 86. Thus at the time of the instant invention, it would have been obvious to the ordinary artisan to make the claimed adenovirus vectors of present claims 67 and 86 given claims 64 and 78 of '320.

Claims 86-89 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 77 of U.S. Patent No. 6,740,320 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because present claims 86-89 are obvious variations.

The present claim is to pharmaceutical compositions comprising adenoviral vectors comprising a wild-type p53 gene operably linked to a promoter (claim 86) and where the promoter is a β-actin, SV40 or RSV (claims 87-89). Claim 77 of '320 are drawn to a pharmaceutical composition comprising a recombinant adenovirus containing an adenovirus vector construct comprising an expression region encoding p53 under the control of a promoter and a pharmaceutically acceptable carrier, expedient or diluent. The pharmaceutical composition of present claims 86-89 contains the same recombinant adenovirus as claim 64 of '320. The specification of '320 defines promoter as including the β-actin, SV40 and RSV promoters. Pharmaceutically acceptable carriers were known in the art at the time of filing and it would be obvious use them in the production of present claim

77. Thus at the time of the instant invention, it would have been obvious to the ordinary artisan to make the claimed adenovirus vectors of present claims 86-89 given claim 77 of '320.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 67 and 86-89 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons presented in the office action mailed September 9, 2003.

Claims 67 and 86-89 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons presented in the office action mailed September 9, 2003.

In summary, the present specification fails to convey that at the time of their earliest claimed priority date, October 13, 1992, that applicant's had possession of the claimed invention. Presently amended claims are to adenoviral vectors comprising a wild-type p53 gene under the control of a promoter, wherein the vector is comprised in a pharmaceutical composition. The claims specifically, state that the promoter can be a CMV, β-actin, SV40 or RSV promoter. It is maintained that the present specification fails to provide sufficient disclosure that applicant's contemplated the claimed adenoviral vectors either figuratively or

specifically. The description disclosed would not allow those of ordinary skill in the art to recognized that the presently claimed adenoviral vectors had been invented by applicant.

Applicant argues that the issue is not whether the specific citations provided by applicant provide written description, but whether the disclosure as a whole provides sufficient description to indicate possession of the claimed vectors at the time of filing. Applicant argues that declarations by those of ordinary skill in the art have been supplied: Dr. Lou Zumstein and Dr. Philip Hands. Applicant argues that the action has not rebutted the evidence presented by these ordinary skilled artisans. Applicant argues that there is a preponderance of evidence as stated in MPEP 2163.04, and thus the rejection should be withdrawn. These arguments are not persuasive.

In previous office actions, an analysis of the specification at the citations given by declarants as evidence of written description was provided. Included was an analysis not only of the citations but also of disclosure before and after the citations. The analysis was performed as a reading of the specification and, thus, more thorough than a reading of declarant's and applicant's specific citations. The opinions of declarants Zumstein and Hands were countered with a clear explanation. This explanation has not been rebutted. (Applicant is referred to previous office actions mailed April 12, 2001, February 12, 2002, September 27, 2002, May 28, 2003 and September 9, 2003)

Applicant argues that adenoviruses are disclosed in the specification more than in the context of antisense RNA production. Applicant argues that adenoviruses are discussed as part of the broader context of the invention disclosed on page 14, lines 9-12. Applicant argues that the following paragraph discussing promoters indeed recites particular embodiments of the invention, such as antisense. Applicant states that the specification states "generally speaking, such a promoter might include either a human cellular or viral promoter" and that the β-actin promoter is the preferred promoter but the invention is not

limited to that promoter (specification, page 14, lines 35 to page 15, line 2). These arguments are not persuasive.

At each of the citations on page 14, the surrounding paragraphs are directed towards retroviral vectors and antisense expression. The disclosure of adenoviruses is within the context of substituting for retroviruses in expressing antisense. Further the context of using promoters other than the β-actin promoter is again with retrovirus expressing antisense. There is no cohesive disclosure that indicates that an adenovirus comprising a gene encoding p53 operably linked to a promoter or anyone of the claimed promoters was conveyed as an invention of applicant.

Thus, the specification fails to convey that applicant had possession of the claimed invention at the time of filing. Thus, are not entitled to the October 13, 1992 filing date. Applicant's, therefore, are entitled only to the filing date of the instant invention, November 23, 1999.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 67 and 86 remain rejected under 3 5 U. S. C. 102(b) as being anticipated by Liu et al (1994) Cancer Research 54, 3662-3667 for reasons presented in the office action mailed September 9, 2003.

Liu teaches an adenovirus vector comprising a wild-type p53 gene operably linked to an CMV promoter (page 3662, col. 2, parag. 4).

Applicant argues that, for the reasons presented in their response to the written description rejection, they are entitled to the early priority date of October 13, 1992, and

thus Liu does not qualify as art against the claimed invention. This argument is not persuasive.

As applicant's arguments regarding the written description rejection were not persuasive, the rejection over Liu et al is maintained.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 86-89 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al (1990) Science 250, 1576-1579 and Stratford-Perricaudet et al (1990) Human Gene Therapy 1, 241-256 in view of Wilkinson et al (1992) Nucleic Acids Res. 20, 2233-2239, Colicos et al (1991) Carcinogenesis 12, 249-255, Rajan et al (1991) J. Virol. 65, 6553-6561 and Hitt et al (1990) Virol. 179, 667-678.

Chen et al teach retroviral vectors comprising a wild type human p53 operably linked to the retroviral LTR (page 1576, col. 3, Figure 1). Chen et al teach that wild type 53 is expressed in transduced Saos cells, and that the transduced cells failed to form colonies on soft agar or tumors in nude mice (page 1577, col. 2, line 12 to col. 3, line 8). Chen et al also teach that wild type p53 counters the transformation phenotype conferred by a mutant p53 when both genes are present in equal gene dosage (page 1579, col. 1, parag. 1 to col. 2, line 1 and col. 2, parag. 1, lines 25-28). Stratford-Perricaudet et al teach the correction of an enzyme deficiency related disorder in mice (abstract). The mice are mutant for ornithine transcarbamylase and when treated with an adenovirus vector comprising an ornithine transcarbamylase DNA sequence operably linked to the adenovirus major late

promoter, the mice exhibit a reversal of the mutant phenotype (page 251, parag. 1, lines 1-3). Chen et al and Stratford Perricaudet et al do not teach adenoviral vectors comprised of a wild type p53 gene under the control of a CMV promoter, a β-actin promoter, an SV40 promoter or an RSV promoter. Wilkinson et al teach the production of an adenovirus expression system where a CMV promoter regulates expression of lacZ (page 2234, col. 1, parag. 5, lines 1-3). Wilkinson et al also teach that the adenovirus-CMV system can be used to studies of gene expression and gene regulation (page 2238, col. 2, parag. 4, lines 1-4). Colicos et al teach an adenovirus vector comprising a T4 *denV* gene operably linked to the RSV promoter, the RSV LTR (page 250, col. 1, parags. 4-7, figure 1 and figure 2). The vector, Ad5denV, was shown to partially complement the excision repair deficiency in primary fibroblasts from xeroderma pigmentosa patients (page 254, col. 1, parag. 2, and page 253, figures 6 and 7, and Table 1). Rajan et al teach an adenoviral vector comprising a cDNA sequence encoding an SV 40 small-t antigen operably linked to an SV40 promoter (page 6554, col. 1, parag. 2). Rajan et al teach that the expression of the SV40 small-t antigen results in the transactivation of adenovirus EII early promoter (page 6557, col. 1, line 13 to col. 2, line 4). Hitt et al teach an adenovirus where the expression of the E1A gene is regulated by a human β-actin promoter (page 670, col. 1, line 12 to col. 2, line 2, and figure 1). Hitt et al teach that E1A production is 3 to 5 times higher than by wild type adenovirus (page 675, col. 2, parag. 1, lines 11-16).

Applicant argues that at the time of filing, the ordinary artisan would not have found a reasonable expectation of success regarding the ability to express p53, particularly in a therapeutic context as the claims recite a pharmaceutical composition. Applicant argues that the claimed adenoviral vectors cannot be claimed and used. Applicant argues that previously supplied references of Jaffee and Rosefeld teach that pharmaceutical compositions comprising Ad-p53 are similarly unpredictable. Applicant argues that the

patent office does not restrict between pharmaceutical compositions and methods of therapy using those compositions. Applicant argues that in a related application, the patent office took the position that gene therapy was unpredictable. Applicant argues that the present rejection is based on gene therapy. Applicant argues that in the early 1990's it was unknown if an adenovirus vector comprising the p53 gene could be made because p53 was known to bind E1B. Applicant argues that to produce the vector, the virus would need to be produced in a host cell, which would require expression of E1B and p53. Applicant argues that it would be unpredictable to even make the vector. These arguments are not persuasive.

The rejection is not based on the argument that the vectors would be obvious for use in a gene therapy protocol to replace p53. Rather the rejection states that the teaching, suggestion and motivation found in the combination of cited art is for the claimed pharmaceutical compositions to be used to assess usefulness in gene therapy. It is the products, the pharmaceutical composition comprising adenovirus, that is claimed; not methods of gene therapy. Restriction is based upon search burden. The lack of a restriction requirement does not address enablement or art rejections. When a restriction/election requirement isn't issued all that means is that there is no search burden on the examiner. As stated in the previous office action, Jaffee and Rosenfeld state that gene therapy methods requiring the replacement of p53 are unpredictable. Jaffee and Rosenfeld never state that the production of adenoviral vectors or pharmaceutical compositions comprising them is unpredictable. If indeed, intact adenoviral vector comprising a gene encoding p53 could not be made because of the production of E1B protein, then applicant should supply a declaration or reference teaching that. However, only one adenoviral vector would need to be made to meet the present claims. Low adenoviral-p53 titers is not relevant to the presently claimed products,

Further it is noted that US Patent 6,740,320 B1 issued May 25, 2004 contains claims to a pharmaceutical composition comprising an adenovirus containing and adenovirus vector construct comprising an expression region encoding p53 under the control of a CMV promoter and a pharmaceutically acceptable carrier, excipient or diluent (claim 64) and a pharmaceutical composition comprising a recombinant adenovirus comprising an adenovirus vector construct comprising an expression region encoding p53 under the control of a promoter, wherein the promoter provides expression sufficient to inhibit tumor cell growth in vivo; and a pharmaceutically acceptable carrier, excipient or diluent (claim 70), with claim 71 stated that the promoter is the CMV promoter. Claims 66 and 86 in the present applicant are essentially the same as issued claims 64, 70 and 71 of '320. Thus applicant is stating that there is no reasonable expectation of success in producing these vectors because of potential binding of produced p53 to the adenovirus E1B protein. Claims 64, 70 and 71 are not limited to an adenovirus unable to produce E1B. Thus, if claims 64, 70 and 71 have a reasonable expectation of success in their implementation then claims 66 and 87 also have the same expectation of success. Further, if the production of E1B is the argument, claims 86-89 also have a reasonable expectation of success in their production and use. It is noted that the specification in '320 discloses the β-actin, SV40 and RSV promoters as being useful in the claimed invention. Applicant cannot say that claims 64, 70 and 71 in '320 have a reasonable expectation of success in being made and use, but the ones in the cited prior art do not have such expectation.

Applicant argues that the combination of cited art would constitute only an obvious to try situation. Applicant argues that the statement in the rejection that the production of the claimed vectors to assess in vivo potential is obvious to try. Applicant argues that *In re Lilly & Co.*, 14 USPq2d 1741, 1743, (Fed. Cir 1990), exists when "the disclosure itself does not contain sufficient teaching of how to obtain the desired result or indicate that the

claimed result would be obtain if certain directions were pursued." Applicant argues that the cited references fail to indicate that sufficient expression of p53 could be achieved in the context of an adenovirus vector and thus qualify as promoting the attempt toward attaining the claimed invention. These arguments are not persuasive.

The claims, in essence, are to pharmaceutical compositions comprising an adenoviral vector comprising a p53 gene operatively linked to a promoter. The "pharmaceutical" adjective is an intended use limitation and is not given patentable weight in an art rejection. However, even if "pharmaceutical" were to be given weight, then the art teaches adenovirus pharmaceutical compositions (Stratford-Perricaudet). Further, the teachings of Stratford-Perricaudet are that assessment of in vivo potential is a reasonable use, or motivation, for making and administering in vivo adenovirus vectors. There is no further research required for assessment; the cited art, and the rejection made previously, provide the teachings, suggestions and motivations to make and use the claimed invention. Applicant should note that the rejection is not that therapy is achieved or that therapy is the teaching, suggestion or motivation. The rejection is that the cited prior art teaching assessing the in vivo potential of an adenovirus vector.

Applicant argues that the claimed invention, to pharmaceutical compositions of adenoviral vectors comprising a gene encoding p53 in the context of gene therapy, have unexpected results in clinical trials. Applicant argues that a declaration by Deborah R. Wilson supported this allegation and was submitted previously in this prosecution. Applicant clarifies that the vector used in the Wilson declaration, INGN 201, is a vector described in a number of patents. Applicant argues that any gene therapy success is surprising and unexpected, and this result could not be predicted on the prior cited in the present obviousness rejection. These arguments are not persuasive.

Applicant's clarification of the vector contained in INGN 201 is not sufficient. Applicant is using INGN to overcome an art rejection. Such information must be made in the form of a declaration, signed by some of direct knowledge. Also, many vectors are disclosed in applicant's issued patents, but which one is INGN 201 is not given. As stated in the office action mailed September 9, 2003, the Wilson declaration at most is persuasive for methods of therapy using a pharmaceutical composition comprising an adenovirus vector comprising a gene encoding p53 operably linked to a CMV promoter; not the pharmaceutical composition. Methods of therapy using the claimed adenovirus vectors are not being examined in this application.

Applicant argues that several patents have issued to them involving adenovirus vectors expressing p53. Applicant states that these patents claim priority to the same application for which priority is claimed in the present application. Applicant argues that the issued patents are evidence that claimed invention is novel and non-obvious. These arguments are not persuasive.

Each of applicant's provided patents and issued claims had been reviewed. However, none of the issued claims are to adenoviral vectors where a p53 gene is operably linked to an β-actin, RSV or SV40 promoter. It should be noted that some of these claim sets are only to methods of treatment. These patents and allowed claims are not relevant to the present prosecution as only products are being examined. Further, these previously allowed claims have no bearing on the prosecution of claims 87, 88 and 89. As for claims 67 and 86, where the claims are to a pharmaceutical composition comprising an adenoviral vector comprising a gene encoding p53 operably linked to a CMV promoter, or broadly to any promoter, each application is judged on its own merits. Comment on other prosecution and what might have been persuasive in other prosecutions is not known.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 571-272-0727. The examiner can normally be reached on M-Th, 8:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 571-272-0408. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Deborah Crouch

Deborah Crouch, Ph.D.
Primary Examiner
Art Unit 1632

June 7, 2004